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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/795,873	03/08/2004	Jean-Pierre Hermet	1049-04	3189

35811 7590 08/06/2009

IP GROUP OF DLA PIPER LLP (US)
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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
08/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pto.phil@dlapiper.com

Office Action Summary	Application No.	Applicant(s)	
	10/795,873	HERMET ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-38* is/are pending in the application.

4a) Of the above claim(s) *11,12,18-22 and 29-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13-17,23-27,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 11-12, 18-22 and 29-36 are withdrawn. Claim 28 is cancelled. Claims 1-10, 13-17, 23-27 and 37-38 are under consideration in this office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-5, 8, 10, 14-17, 23-27 and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., (US Patent 5,766,552) and Aunet et al., (US Patent 4,933,092) in view of Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77).

The claims are drawn to a method for detecting contaminating microbes possibly present in a blood product comprising blood cells comprising: a) subjecting a sample of the blood product to an aggregation treatment of the blood cells, b) substantially eliminating aggregates formed in step (a) by passage of the sample over a first filter allowing passage of contaminating microbes, but not cell aggregates, c) selectively lysing residual cells of the filtrate obtained in step (b), d) adding a marker agent to label the contaminating microbes either during step (a) or step (b), e) recovering the contaminating microbes by passage of the lysate from step (c) over a second filter with

a pore size of about 0.3um to less than 1um which retains contaminating microbes and allows passage of cellular debris, and f) analyzing material on the second filter to detect labeled contaminating microbes possibly retained by the second filter, the method being performed in an enclosed and sterile device.

Doshi et al., teach that the separation of serum or plasma from whole blood is extremely important since it is difficult to conduct the analysis of dissolved blood components without interference from red blood cells (col. 1, lines 47-50). Red blood cells (RBC) are removed from whole blood samples by contacting a whole blood sample with an agglutinating agent (col. 7, lines 25-28). The agglutinating agents allow for the quick and efficient formation of clusters of RBC, be fast acting, have short reactivation time, are non-specific to blood types, and be stable and inexpensive (col. 5, lines 32-34). Doshi et al., teach antibodies as agglutinating agents since they are reactive and well known for agglutinating erythrocytes (col. 7-8, lines 66-6). These antibodies should recognize antigenic surface constituents such as glycoproteins (col. 8, lines 6-10).By contacting the RBC with agglutinating agent, the cells are agglutinated and trapped by the pad while the remainder of the fluid sample flows through readily (col. 6, lines 10-15). Doshi et al., teach the efficiency of filtration, along with the lysis of RBC wherein whole blood is passed through the filter and plasma is retained (col. 8, lines 54-56). Doshi et al., teach the removal of the RBC clusters by filtration (col. 11, lines 40-41). The preferred filtration uses a porous absorbent pad with mesh or pore size being from about 20 to about 500 microns (col. 62-65). This is within the instantly claimed size of pores for the first filter. The secondary filter is used to trap red blood cells and has a

very small pore size to permit plasma to pass (col. 12, lines 1-11). Doshi et al., teach having a reactant pad through which the fluid flows to allow for the production of a detectable signal (col. 14, lines 39-41). The analyte reacts with the reagents to produce a detectable signal such as dyes, particles, and proteins with visible extinction coefficients (col. 14, lines 42-43). Thus, where the analyte is an enzyme substrate, the pad may be impregnated with the appropriate enzyme or enzymes to produce a product that is measured (col. 15, lines 10-13). The production of a detectable signal produced by enzymes teach the marker agent. The method teaches a measurement dye zone wherein the zone is coated or impregnated with an indicator material that reacts with the enzyme treated sample to give an indication of the presence or amount of analyte in the sample (col. 16, lines 23-27). Thus the indicator material that reacts with the enzyme treated sample material is the marker agent.

Doshi et al., teach one type of RBC agglutinating agent is lectins, including *Phaseolous vulgaris* (col. 7, lines 46-48). Other agglutinating agents include antibodies that have a binding affinity for a determinant present on the surface of red blood cells that recognizes antigenic surface constituents (col. 7-8, lines 65-8). Doshi et al, teach a minimum amount of antibody must be used in the blood separation device (col. 8, lines 43-45). Doshi et al., state that one skilled in the art will readily determine the optimum amount of antibody to be used in the method (col. 8, lines 49-51). Thus Doshi et al., teach using an appropriate concentration of antibody. The use of detergents where a lipophilic analyte is in the blood is disclosed (col. 15, lines 27-28). The detergents are anionic or cationic detergents (col. 15, lines 33). Thus the art teaches using cationic and

anionic detergents. Doshi et al., teach using various sticking agents or adhesives (col. 15, lines 38-41). These sticking agents would meet the permeabilization agents. However, Doshi et al., do not teach the method being performed in an enclosed and sterile device and comprising selectively lysing the cells and recovering microbes with second filter having a pore size of about 0.3um to less than 1um which retains contaminating microbes and allows passage of cellular debris.

Aunet et al., teach agglutination and separation of blood products including devices and techniques. Aunet et al., teach subjecting a sample of the blood product to an aggregation treatment of the blood cells (col. 2, lines 56-63). Aunet et al., teach substantially eliminating aggregates formed by passage of the sample over a first filter (col. 3, lines 9-11). Aunet et al., teach a device comprising an enclosed and sterile housing, entry and exit ports 9col. 5-6, lines 67-3). See also Figures 1-2.

Zierdt et al., teach selectively lysing the cells and recovering microbes with second filter having a pore size of about 0.3um to less than 1um which retains contaminating microbes and allows passage of cellular debris (page 74 col. 2 and page 75, col.1). Zierdt et al., running the lysed blood samples through a filter sized at 0.45um which thereby has a pore size of about 0.3um to less than 1um and can retain contaminating microbes yet allow passage of cellular debris (page 75, col.1). Zierdt et al., teach the superiority of the lysis-filtration procedures (page 75, col. 2). Zierdt et al., teach increased sensitivity in the detection of bacteremia (page 77, col. 1). Zierdt et al., teach techniques were blood sample was treated with a lysing solution to release intracellular bacteria and then membrane filtered which had the advantage of separating

bacterial pathogens from all antibacterial properties of the blood including antibodies, complement, phagocytes and antibiotics (page 74, col.1).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et al., to include an enclosed and sterile device of Aunet et al., and the lysing step and second filter that retains contaminating microbes and allows passage of cellular debris as taught by Zierdt et al., because Zierdt et al., teach that the lysis reaction increases the amount of bacteria retained by the filter and thereby removed from the blood; while Aunet et al, teach a safe device to allow blood analysis without contamination. No more than routine skill would have been necessary to include an enclosed device, a lysis reagent and step in the method of detection, since the art teaches that it is desirable to rid a blood sample of substantially all blood cells since it is difficult to conduct an analysis of the blood components without interference from external sources and red blood cells when testing for microbial contamination. Moreover, there would have been a reasonable expectation of success in this modification since the art teaches that the lysis reagent and step does not harm the contaminants yet prepares the blood sample for microbial detection and analysis without time consuming and expensive techniques. Finally it would have been obvious to incorporate the enclosed device of Aunet et al., and the lysis and second filter of Zierdt et al., into the method of detection as taught by Doshi et al., because the lysing solution is known to release intracellular bacteria and filtration is advantageous because it separates out bacterial pathogens without allowing further contamination from external

sources; thus yielding predictable results to one of ordinary skill in the art at the time of the invention.

Response to Arguments

4. Applicant's arguments filed May 19, 2009 have been fully considered but they are not persuasive.

The rejection of claims 1-5, 8, 10, 14-17, 23-28 and 37-38 under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., and Aunet et al., in view of Zierdt et al., is maintained for reasons already of record.

Applicants assert that housing, inlet and exit ports disclosed by Aunet et al., are not enclosed and sterile. However applicants is reminded that the claims recites "said method is performed in an enclosed and sterile device. Therefore any person of ordinary skill performing analysis on blood or blood products would perform the assay within a sterile and enclosed hood.

The claims are drawn to a method of detection and require that the method be performed in an enclosed and sterile device. In response to applicants assertion, the rejection based upon the teachings of Doshi et al., Aunet et al., and Zierdt et al., teach the use of housing, inlet and exit ports. Clearly, the purpose of an inlet port is to control assess to an enclosed and sterile environment where the assay occurs. All of the art of records is drawn to filtration procedures, the elimination of contaminants, removal of foreign particulates, and the separation of unwanted molecules to thereby provide a sterile testing environment. Thus the environment provided the prior art rejections is

sterile based upon separation techniques which is extremely important since it is difficult to conduct without interference. Aunet et al., specifically states that located within the housing is a device which performs the assay and where access to the device is by the inlet port, thus the device is clearly enclosed.

Applicant assert that there is no teaching drawn to the sample being introduced into a closed or sterile device. However Applicant is reminded that the claims do not require sample being introduced into an enclosed and sterile device. Rather the claims merely require that the method is performed in an enclosed and sterile device; thus there is no limitation on sample introduction. Therefore the argument is not persuasive.

Applicants assert that the Figures of Aunet et al., are not enclosed or sterile. However Aunet et al., teach a housing which not only holds but encloses the device matrices whereby the only means for sample being introduction to the porous matrices is by the inlet port. Aunet et al., also teach an exit port for which the sample to exit. Thus the matrices are clearly enclosed since the only way for sample to enter and exit is by the inlet and exit port. Furthermore, the matrices are within the housing; therefore if the matrices are within the housing then it is the position of the Office that the matrices are enclosed. Therefore Applicants assertion that the matrixes are open to ambient atmosphere is not persuasive.

Applicants assert that the matrix (42) in Figure 2 is exposed to ambient atmosphere, however there is clearly a covering other the matrix as evidenced by (37). Furthermore, in the Figure Aunet et al., shows an entry port (33) and the inlet (34) and the exit vent (36). Therefore contrary to Applicants assertion the matrix is not open to

ambient atmosphere and the only access to the matrix is the port. Furthermore the entry and exit port are clearly within the housing; thus applicants' argument is not persuasive.

Additionally, housing protects matrices and clearly provides a sterile environment for which the method is performed.

Applicants' mere arguments that an enclosed and sterile Applicants have provided no evidence that there are any contaminants from the surrounding environment.

Therefore applicants' arguments is not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

5. Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable Doshi et al., (US Patent 5,766,552) and Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77) further in view of Cathey et al., (US Patent 5,798,215).

The claims are drawn to a method for detecting contaminating microbes comprising a marker agent that comprises a fluorescent marker or an agent coupled to a flurochrome or an enzyme enabling degradation of substrate thereby made fluorescent wherein the fluorescence is produced using an excitation laser and detected.

The teachings of Doshi et al., and Zierdt et al., have been discussed above. However neither teaches a fluorescent marker or an agent coupled to a flurochrome or an enzyme enabling degradation of substrate thereby made fluorescent wherein the

fluorescence is detected by an excitation laser wherein the method is performed in an enclosed and sterile device.

Cathey et al., teach analyte detection assays wherein the assay platform comprises a filter (col. 6, lines 19-21). The separation means for separating sample components may be positioned in the flow path of the assay platform (col.6, lines 54-56). For example, a filter may be positioned such that in when samples comprise red blood cells, the red blood cells are retained while serum flows through the filter (col. 6, lines 56-60). Depending upon the nature of the sample, the sample may be subjected to prior treatment, such as filtration or cell separation (col. 12, lines 15-19). For blood, one may wish to remove red blood cells to provide plasma or serum (col. 12, lines 20-21). Upon substrate addition, the substrate flows into the main flow path, where it is converted by an enzyme to a detectable product (col. 14, lines 34-36). Cathey et al., the method being performed in an enclosed and sterile housing comprised within the device (Figures 1,2 and 4). Fluorescent labels or enzymes are preferred because they convert substrates to non-diffusible dyes that are used in signal producing systems (col. 13, lines 60-64). These signal systems also provide for wider testing capabilities and are useful in microbial detection/diagnosis (col. 13, lines 64-66). Optical signals which may be detected and related to the presence and/or amount of analyte in the sample include emissions, e.g. from fluorescent labels or the fluorescence of a quenching member of a signal producing system (col. 14, lines 53-56). The optical signals are detected by a wide variety of means including devices that measure absorbance, transmissions, diffraction, resonance which includes lasers (col. 15, lines 13-34).

Therefore no more than routine skill would have been necessary to include a fluorescence marker in the method of detection, since the art teaches that it is desirable to use fluorescence detection signals to detect analytes and other microbes. Moreover, there would have been a reasonable expectation of success in this modification since only routine skill would have been required to use fluorescent agents coupled with an enzyme substrate when Doshi et al., already teach microbial detection with enzymatic substrates.

Response to Arguments

6. Applicant's arguments have been fully considered but they are not persuasive.

The rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable Doshi et al., and Zierdt et al., further in view of Cathey et al, is maintained for reasons of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). It is noted that Doshi et al., Aunet and Zierdt et al., have been discussed above. In this case, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et

al., and Zierdt et al., to include a marker agent that comprises a fluorescent marker or an enzyme enabling degradation of substrate thereby made fluorescent wherein the fluorescence is detected by an excitation laser in an enclosed and sterile device whereby the method is performed as taught by Cathey et al. because Cathey et al., teach that fluorescent labels convert substrates to non-diffusible dyes are used in signal producing systems by performing the method in a enclosed and sterile device. Therefore, Applicants arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

7. Claims 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., (US Patent 5,766,552), Aunet et al., (US Patent 4,933,092) and Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77) further in view of Besson-Faure et al. (US Patent 6,168,925).

The claims are drawn to a method for detecting contaminating microbes comprising a specific antibody to a platelet antigen such as anti-GpIIb/IIIa.

Doshi et al., Aunet et al., and Zierdt et al., have been discussed above however neither teaches a specific antibody to a platelet antigen such as anti-GpIIb/IIIa.

Besson-Faure et al., teach the anti-GpIIb/IIIa antibody as a specific antibody to a platelet antigen that causes aggregation. Besson-Faure et al., teach the analysis of platelet GpIIb/IIIa receptors (col. 1, lines 5-8). Activated platelets have this receptor which binds with very high affinity and causes aggregation of the platelets with each

other (col. 1, lines 25-30). The activation of the platelets allows the receptor to bind with high affinity, which causes aggregation (col. 1, lines 27-31). The molecules also remain in circulation for long periods of time (col. 1, lines 57-60). Besson-Faure et al., teach anti-GpIIb/IIIa antibodies are publicly available (col. 3, lines 1-10).

No more than routine skill would have been necessary to include anti-GpIIb/IIIa in the method of detection, since the Doshi, Aunet et al., and Zierdt et al., teach that it is desirable to use antibody agglutinating agents that are quick, efficient at cluster formation, and fast acting and Besson-Faure et al., teach the anti-GpIIb/IIIa agglutinating agent which efficiently causes high affinity agglutination. Moreover, there would have been a reasonable expectation of success in this modification since only routine skill would have been required to use antibodies as agglutinating agents when the prior art provides motivation for antibody agglutinating agents wherein the motivation is that antibodies are reactive, well known for agglutinating properties and recognize glycoproteins; and Besson-Faure et al., provide commercially available anti-GpIIb/IIIa agglutinating antibodies that cause high affinity agglutination.

Response to Arguments

8. Applicant's arguments have been fully considered but they are not persuasive.

The rejection of claims 9 and 13 under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., Aunet et al., and Zierdt et al., further in view of Besson-Faure et al., is maintained for reasons already of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). It is noted that Doshi et al., Aunet and Zierdt et al., have been discussed above. Thus, in this case, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et al., Aunet et al., and Zierdt et al., wherein the method is performed in an enclosed and sterile device and the method further includes anti-GpIIb/IIIa antibody as a specific antibody to a platelet antigen as taught by Besson-Faure et al., because Besson-Faure et al., teach the a superior aggregation properties of anti-GpIIb/IIIa. Therefore applicants' arguments are not persuasive and the rejection is maintained.

Conclusion

9. No claims allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/

Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645